UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

HA

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/082,112	05/20/98	MENDOZA A	MSU4.1-406

IAN C MCLEOD
2190 COMMONS PARKWAY
OKEMOS MI 48864

HM22/0813

EXAMINER	
TURNER, S	
ART UNIT	PAPER NUMBER
1647	32

DATE MAILED: 08/13/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/082,112	Mendoza
Examiner	**Art Unit**
Sharon L. Turner, Ph.D.	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 6-4-01

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 16-25 is/are pending in the applica

4a) Of the above, claim(s) _____ is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 16-25 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

Response to Amendment

Request for Continued Examination

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6-4-01 has been entered.

2. The amendment filed 6-4-01 has been entered into the record and has been fully considered.

3. Claims 16-25 are pending.

Claim Objections

4. Claim 25 is objected to because of the following informalities: the claim is lacking a modifier between precipitated and acetone. Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claims 16 and 18 recite the limitation "the disease" where no disease is specified. Applicant's should either reference pythiosis as "the disease" or recite pythiosis.

8. Claim 17 recites the limitation "the vaccination" in reference to claim 16. There is insufficient clear antecedent basis for this limitation in the claim as a "vaccination" is not recited in the claim. Claim 16 and 17 should utilize consistent terminology.

9. Claim 19 and 24 recite "removing the disrupted cells to provide the mixed intracellular proteins". Such recitation is indefinite to the skilled artisan as to what is being removed or what steps are being performed. Applicant's are suggested to recite a step which may be discerned by the artisan such and removing insoluble material by centrifugation.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 16-25 stand rejected under 35 U.S.C. 103(a) as set forth in Paper Nos. 23, 26 and as set forth herein as being unpatentable over Mendoza et al, J. Mycol. Med, 1996, 6:151-164, Mendoza et al, Mycopathologica, 1992(a), 119:89-93, (IDS: Ref. AI), Mendoza et al, J. Clin. Microbiology, Nov. 1992(b), p. 2980-83, Sigma Catalog, p.1874, 1992, Amicon Catalog, p. 35, 1993 and Mendoza et al., Abstract, Third NIAID Workshop in Medical Mycology Series, September 7-9, 1995.

The specification describes at page 6, line 15, that the improved vaccine (was) prepared by adding cytoplasmic antigens to the earlier *P. insidiosum*-vaccine (Mendoza et al., Mycopathologica 119:89-95 (1992(a))). Mendoza et al, 1992(a) disclose two prior art vaccines, a cell-mass vaccine (CMV) and a soluble concentrated antigen vaccine (SACV). Based on the guidance in Example 1 it is understood that the isolated antigens were added to the SCAV vaccine of Mendozas earlier publication in 1986 which corresponds to the SCAV vaccine. This is the vaccine which applicant's assert exhibit unexpected results in chronically infected horses and is the vaccine which was used to treat the human patient in Example 4.

The claims do not recite the teachings of the specification with respect to the preparation of the improved vaccine, i.e., isolation of the proper cytoplasmic antigens which are to be added to the vaccine. Neither of the vaccines of Mendoza et al., 1992(a) are the vaccines as disclosed in Example 1 as neither of the prior art vaccines has isolated cytoplasmic antigens added to the preparations. However, the specification in Example 1 references that the prominent cytoplasmic antigens were added as describe in Mendoza et al., J. Clin. Microbiol., 30:2980-2983, 1992(b). Mendoza et al., Abstract 1995, teaches that the addition of 28-32 kD immunodominant peptides to culture filtrate proteins leads to the cure of 8 chronically infected horses. As discussed, the Mendoza et al., 1992(b) reference teaches these cytoplasmic antigens and thus provides the improved vaccine.

In contrast to the description of the improved vaccine in the specification, the claims recite a vaccine which is distinct from the exemplary vaccine of the specification with added

cytoplasmic antigens. In particular, the vaccine of the specification is the addition of the three isolated immunodominant proteins purified from a CMV preparation added to the SCAV vaccine of Mendoza and appears to be the same as that of Mendoza et al., 1995. This vaccine is different from the vaccine claimed in that the claimed vaccine is essentially a combination, a vaccine which combines the elements of the CMV and SCAV preparations (mixed intracellular and extracellular proteins) of the prior art. The methodology disclosed for the preparation of the two vaccines and the isolation of the three added immunodominant peptides are referenced at p. 2981, column 1 as disclosed in Mendoza et al., J. Clin. Microbiol., 30:2980-83, 1992 and as referenced by the specification. Mendoza in this publication clearly evidences that the three immunodominant proteins which are added to the improved vaccine are present in the CMV preparation, represent immunodominant peptides and further suggests that such peptides may be useful for diagnostic and immunotherapeutic effects in horses, see in particular abstract and 2981, column 1. It is thus noted that the reference evidences the presence of the isolated immunodominant peptides in the CMV preparation. It is further noted that the 1995 abstract renders obvious the treatment of chronically infected horses with such vaccine.

Thus in summary and as previously set forth, the prior art teaches two vaccines the CMV and SACV vaccines which are known to be useful and effective in the treatment of pythiosis infection in horses. Consistent with case law and as set forth in the MPEP 2144.06, "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose... [T]he idea of combining them flows logically from their having been

individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980)."

Applicant's remarks in response to the previous rejection of record include the following arguments: (1) that the claim amendments regarding the terms "intracellular" and "extracellular" as supported at p. 3, lines 3-7 and 3-15 are operational terms understood by the skilled artisan as terms which describe the destination where the proteins are to ultimately reside. It appears to be applicant's contention that such amendments to the claims remove the prior art references from that encompassed by the claims, and in particular that the additionally recited steps render the composition superior, (2) that a PM-10 membrane does not remove low molecular weight contaminants and that (3) the protective effect in humans is unexpected.

Applicant's arguments filed 6-4-01 have been fully considered but are not persuasive because the prior art references disclose vaccines comprising intracellular and extracellular proteins, see in particular Mendoza et al., 1996, p. 159, column 2, lines 15-18, and Mendoza et al., 1992(a) or Mendoza et al., 1992(b) for comparisons of the cell-mass vaccine and soluble concentrated antigen vaccines, in particular Mendoza et al., 1992(a), Vaccine preparation, pp. 90-91 and Mendoza et al., 1992(b), Materials and Methods, p 2980-2981. In addition the improved vaccine is recognized for the treatment of chronically infected horses. The process limitations of filtration via ultracentrifugation or a stir cell through a PM-10 membrane remove small peptides and impurities as set forth previously and in particular is evidenced by Table 19 of the provided Amicon catalog p. 35. This step is an obvious equivalent which does not appear to result in a

patentably distinguishable product from that of dialysis to remove small peptides and impurities because the molecular weight cut offs for the PM-10 membrane and a dialysis membrane are similar as evidenced by Sigma, Amicon and Mendoza et al., 1992(b) as set forth at p. 8-9 of the office action of 11-7-00, Paper No. 26 and as set forth herein. The previous office action sites Sigma for dialysis tubing with a molecular weight cutoff of approximately 12,400 MW and PM-10 membrane of MW cut-off of 10,000 MW. The examiner provides herein the MW of Thimerosal as evidenced by Sigma, p. 952 of 404.8 MW and thus it is clear that Thimerosal would be removed by either dialysis or ultracentrifugation through a PM-10 membrane. Mendoza 1996, 1992(a) and 1992(b) establishes a similar relationship between the infectious organisms, pathogenesis, evoked immune response (immunodominant epitopes) and serodiagnosis of P. Insidiosum in horses and humans as disclosed in the prior art references. In addition Mendoza 1996 discloses a recognition in the art of standard immunodiagnostic tests which similarly relate P. Insidiosum infection in humans and horses. Thus, in contrast to applicant's assertion, the art recognizes a similarity in horses and humans in Pythiosis infection. Thus, as previously set forth, the skilled artisan would have an expectation of success in immunization of humans with the equine vaccine. In particular it is noted that the unexpected result of synergism which allow protection in horses infected for greater than two months is obvious based on the Mendoza 1995 reference. There is no evidence that humans or other mammals are refractory to treatment of Pythiosis with the combination vaccine which is prima facie obvious and does not appear to exhibit unexpected results in either humans or other mammals. All steps as claimed are met by

the prior art teachings and it would be well within the skill of the artisan to combine the two vaccine preparations together as claimed. Thus, the cumulative reference teachings anticipate the claimed invention.

Status of Claims

12. No claims are allowed.

Conclusion

13. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached at (703) 308-4623.

Sharon L. Turner, Ph.D.
August 12, 2001

GARY L. KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600